This Page Is Inserted by IFW Operations and is not a part of the Official Record

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

IMAGES ARE BEST AVAILABLE COPY.

As rescanning documents will not correct images, please do not report the images to the Image Problem Mailbox.

Continuation of Application No.: 10/149,549

IN THE CLAIMS:

formula

Ì,

Claim 1 (currently amended and reformatted): A compound of general

$$R^2$$
 R^3
 R^1
 R^3
 R^3

wherein D represents CH₂ or CH₂CH₂;

E represents C(O)NH or NHC(O);

 R^1 and R^2 each independently represent hydrogen, halogen, amino, nitro, $C_1\text{-}C_6$ alkyl or trifluoromethyl, but R¹ and R² may not both simultaneously represent hydrogen; R³ represents a group of formula

$$R^4 X R^5$$
 (II);

R⁴ represents a C₁-C₆ alkyl group;

X represents an oxygen or sulphur atom or a group NR 13, SO or SO2;

ATTORNEY DOCKET NO.: 056291-5103-01 Continuation of Application No.: 10/149,549

Page 4

R⁵ represents hydrogen, or R⁵ represents C₁-C₆-alkyl or C₂-C₆-alkenyl, each of which may be optionally substituted by at least one substituent selected from halogen, hydroxyl, (di)-C₁-C₆-alkylamino, -Y-R⁶,

,c

a 5 or 6-membered heteroaromatic ring comprising from 1-to 4 heteroatoms independently selected from nitrogen, oxygen and sulphur which heteroaromatic ring may itself be optionally substituted by at least one substituent selected from halogen, hydroxyl and C₁-C₆-alkyl;

Y represents an oxygen or sulphur atom or a group NH, SO or SO2;

 R^6 represents a group $-R^7$ Z where R^7 represents a C_2 - C_6 alkyl group and Z represents an -OH, $-CO_2H$, $-NR^8R^9$, $-C(O)NR^{10}R^{11}$ or $-N(R^{12})C(O)$ - C_1 - C_6 alkyl group, and, in the case where Y represents an oxygen or sulphur atom or a group NH, R^6 additionally represents hydrogen, C_1 - C_6 alkyl, C_1 - C_6 alkylcarbonyl, C_1 - C_6 alkoxycarbonyl, $C(O)NR^{14}R^{15}$, $-CH_2OC(O)R^{16}$, $-CH_2OC(O)OR^{17}$ -or $-C(O)OCH_2OR^{18}$;

 R^8, R^9, R^{10}, R^{11} and R^{12} each independently represent a hydrogen atom or a C_1 - C_6 -alkyl group;

ATTORNEY DOCKET NO.: 056291-5103-01

Continuation of Application No.: 10/149,549

Page 5

 R^{13} represents hydrogen, C_3 - C_8 cycloalkyl, C_3 - C_8 cycloalkylmethyl, or R^{13} represents a C_1 - C_6 alkyl group optionally substituted by at least one substituent selected from hydroxyl and C_1 - C_6 alkoxy; and

 R^{14} , R^{15} , R^{16} , R^{17} and R^{18} each independently represent a C_1 - C_6 alkyl group; with the proviso that when E is C(O)NH, X is <u>not-O</u>, NH or N(C₁-C₆ alkyl), then R^5 is other than a hydrogen atom or an unsubstituted C_1 - C_6 alkyl group; or a pharmaceutically acceptable salt or solvate thereof.

Claim 2 (original): A compound according to claim 1, wherein D represents CH₂.

Claim 3 (currently amended): A compound according to claim 1 or claim 2, wherein E represents NHC(O).

Claim 4 (currently amended): A compound according to any one of claims 1 to 3 claim 1, wherein R^1 and R^2 each independently represent a hydrogen, chlorine or bromine atom, or an amino, nitro, C_1 - C_3 alkyl or trifluoromethyl group.

Claim 5 (cancelled).

•

Claim 6 (currently amended): A compound according to claim 1-5, wherein X represents a group NR¹³ in which R¹³ represents hydrogen, -(CH₂)₂OH, methyl, ethyl, n-propyl, isopropyl, n-butyl, n-pentyl, n-hexyl, cyclopropyl, cyclopentyl, cyclohexyl or cyclohexylmethyl.

Claims 7-9 (cancelled).

Claim 10 (currently amended and reformatted): A compound of formula (I), or a pharmaceutically acceptable salt or solvate thereof, according to claim 1 which is selected from:

- 2-Chloro-5-[[2-(2-hydroxy-ethylamino) ethylamino]-methyl]-N (tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-benzamide dihydrochloride,
- 2-Chloro-5-[[2-(2-hydroxyethoxy)ethylamino]methyl]-N-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-benzamide,
- 2-Chloro-5-[(3-hydroxy-2,2-dimethylpropylamino)methyl]-*N*-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-benzamide,
- 2-Chloro-5-[(5-hydroxypentylamino)methyl]-*N*-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-benzamide,
- 2 Chloro-5 [[2-[(2-hydroxyethylthio)ethylamino]methyl]-N (tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl) benzamide,
- 2-Chloro-5-[3-[(2-hydroxyethyl)amino]propyl]-*N*-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-benzamide, acetate salt,

2-Chloro-5-[3-[(3-hydroxypropyl)amino]propyl]-*N*-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-benzamide, hydrochloride salt,

•

- 2-Chloro-5-[3-(methylamino)propyl]-N-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-benzamide, acetate salt,
- 2-Chloro-5-[3-[(1-methylethyl)amino]propyl]-*N*-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-benzamide, hydrochloride salt,
- 5-[3-[(2-Amino-2-methylpropyl)amino]propyl]-2-chloro-*N* (tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl) benzamide, dihyrdrochloride salt,
- 2-Chloro-5-[3-[(4-hydroxybutyl)amino]propyl]-*N*-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-benzamide,
- 2-Chloro-5-[3-[(2-hydroxy-2-methylpropyl)amino]propyl]-*N*-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-benzamide, acetate salt,
- 2-Chloro-5-[3-[[2-(methylamino)ethyl]amino]propyl]-N-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-benzamide, dihydrochloride salt,
- (S)-2-Chloro-5-[3-[(2-hydroxypropyl)amino]propyl]-N-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-benzamide, hydrochloride salt,
- (R)-2-Chloro-5-[3-[(2-hydroxypropyl)amino]propyl]-N-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-benzamide, hydrochloride salt,
- (R)-2-Chloro-5-[3-[(2-hydroxy-1-methylethyl)amino]propyl]-N-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-benzamide, hydrochloride salt,
- 2-Chloro-5-[3-[[2-hydroxy-1-(hydroxymethyl)-1-methylethyl]amino]propyl]-N-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-benzamide,

5-[3-[[2 (Acetylamino)ethyl]amino]propyl]-2-chloro-N-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl) benzamide, hydrochloride salt,

3

- 2-Chloro-5-[3-[[2-(diethylamino)ethyl]amino]propyl] N-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-benzamide, dihydrochloride salt,
- 2-Chloro-5-[3-[(3-methoxypropyl)amino]propyl]-N-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-benzamide, hydrochloride salt,
- 2-Chloro-5-[3-[(3-hydroxy-3-methylbutyl)amino]propyl]-N-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-benzamide, hydrochloride salt,
- 2-Chloro-5-[3-[(2-methoxyethyl)amino]propyl]-N-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-benzamide, hydrochloride salt,
- 2-Chloro-5-[[3-(methylamino)propoxy]methyl]-N (tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl) benzamide,
- 2-Chloro-5-[[2-[(2-hydroxyethyl)amino]ethoxy]methyl] N-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-benzamide, acetic acid salt,
- 2-Chloro-5-[[2-[(3-hydroxypropyl)amino]ethoxy]methyl]-N (tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl) benzamide, acetic acid salt,
- 2-Chloro-5-[[[3-[(1-methylethyl)amino]propyl]amino]methyl]-N-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-benzamide,
- 5-[[(3-Aminopropyl)amino]methyl]-2-chloro-N-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-benzamide,
- 2-Chloro-5-[[[2-[(1-methylethyl)amino]ethyl]amino]methyl]-N-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-benzamide,



- 3-[[3-[4-Chloro-3-[[(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)amino]carbonyl]phenyl]propyl]amino]propanoic acid, 2,2 dimethylpropyl ester,
 trifluoroacetic acid salt,
- 5-(2-Aminoethyl)-2-chloro-N-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)benzamide,
- 2-Chloro-5-[3-[(2-hydroxyethyl)pentylamino]propyl]-N-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-benzamide,
- 2-Chloro-5-[3-(methyl-2-propenylamino)propyl]-N-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-benzamide;
- 2-Chloro-5-[3-[[2 (dimethylamino)ethyl]methylamino]propyl] N-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-benzamide,
- 5-[3-(Butylethylamino)propyl] 2-chloro-N-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-benzamide,
- 2-Chloro-5-[3-(methylpentylamino)propyl] N-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)benzamide,
- 2-Chloro-5-[3-[[2-(diethylamino)ethyl]ethylamino]propyl]-N-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-benzamide,
- 2-Chloro-5-[3-[(2-hydroxyethyl)methylamino]propyl]-N-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl) benzamide,
- 2-Chloro-5-[3-(dipropylamino)propyl]-N-(tricyclo[3.3.1.1^{3,7}|dec-1-ylmethyl)-benzamide,
- 2 Chloro-5 [3-[(2-hydroxyethyl)(1-methylethyl)amino]propyl] N (tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl) benzamide,
- 5-[3-[Butyl(2-hydroxyethyl)amino]propyl]-2-chloro N (tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl) benzamide,

Continuation of Application No.: 10/149,549

- 2-Chloro-5-[3-(diethylamino)propyl]-N-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-benzamide,
- 2-Chloro-5-[3-(dimethylamino)propyl]-N-(tricyclo[3.3.1.1^{3,7}]dec-1-vlmethyl)-benzamide.
- 5-[3-(Butylmethylamino)propyl]-2-chloro-N-(tricyclo[3.3.1.1^{3,7})dec-1-vlmethyl)benzamide.
- 2-Chloro-5-[3-[(2-hydroxyethyl)propylamino]propyll-N-(tricyclo[3,3,1,1^{3,7}]dec-1ylmethyl)-benzamide,
- 2-Chloro-5-[3-[ethyl(2-hydroxyethyl)amino]propyl]-N-(tricyclo[3.3.1.1^{3,7}]dec-1ylmethyl)-benzamide,
- 2-Chloro-5-[3-(dibutylamino)propyl]-N-(tricyclo[3.3.1.1^{3,7}|dec-1-vlmethyl)-benzamide.
- 2-Chloro-5-[3-(ethylpropylamino)propyl]-N-(tricyclo[3.3.1.1^{3,7}]dec-1-vlmethyl)benzamide.
- 2-Chloro-5-[3-[methyl(1-methylethyl)amino]propyl]-N-(tricyclo[3.3.1.1^{3,7}]dec-1ylmethyl)-benzamide.
- 2-Chloro-5-[3-[[3-(dimethylamino)propyl]methylamino]propyl]-N-(tricyclo[3.3.1.1^{3,7}|dec-1-vlmethyl)-benzamide.
- 2-Chloro-5-[3-[cyclohexyl(2-hydroxyethyl)amino]propyl]-N-(tricyclo[3.3.1.1^{3,7}]dec-1ylmethyl)-benzamide,
- 2-Chloro-5-[3-(cyclohexylmethylamino)propyl]-N-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)benzamide,
- 2-Chloro-5-[3-(cyclohexylamino)propyl]-N-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)benzamide,
- 2-Chloro-5-[3-[[1-(hydroxymethyl)-2,2-dimethylpropyl]amino]propyl]-N-(tricyclo[3.3.1.1^{3,7}]dec-1-vlmethyl)-benzamide.

Continuation of Application No.: 10/149,549

- 2-Chloro-5-[3-(cyclopropylamino)propyl]-N-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-benzamide,
- 2-Chloro-5-[3-[[2-(dimethylamino)ethyl]amino]propyl]-N-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl) benzamide,
- 2-Chloro-5-[3-[(3-hydroxy-2,2-dimethylpropyl)amino]propyl]-N-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-benzamide,
- 2-Chloro-5-[3-[(1,1-dimethylethyl)amino]propyl]-N-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-benzamide,
- 2-Chloro-5-[3-[[3-(dimethylamino)propyl]amino]propyl]-N-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-benzamide,
- 2-Chloro-5-[3-(cyclopentylamino)propyl]-N-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-benzamide,
- 2-Chloro-N-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-5-[3-[(1,2,2-trimethylpropyl)amino]propyl]-benzamide,
- 5-[3-(Butylamino)propyl]-2-chloro-N-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-benzamide,
- 2-Chloro-5-[3-[[1-(hydroxymethyl)-2-methylpropyl]amino]propyl]-N-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-benzamide,
- 2-Chloro-5-[3-[(1-methylpropyl)amino]propyl]-N-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-benzamide,
- 2 Chloro 5 [3-[[2 (methylthio)ethyl]amino]propyl] N (tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-benzamide,
- 2-Chloro-5-[3-[(2-hydroxy-1,1-dimethylethyl)amino]propyl]-N-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-benzamide,

- 2-Chloro-5-[3-[(cyclohexylmethyl)amino]propyl]-N-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-benzamide, and
- 2-Chloro-5-[3-(2-propenylamino)propyl]-N-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-benzamide;
- 2 Chloro-5-[3-[(2-fluoroethyl)amino]propyl] N (tricyclo[3.3.1.1^{3,7}]dec 1-ylmethyl)-benzamide;
- 2-Chloro-5-[3-[(2-methoxy-1-methylethyl)amino]propyl]-N-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-benzamide.;
- 2-Chloro-5-[3-[3-(methylamino)propoxy]propyl] N (tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)benzamide, dihydrochloride salt,
- 5-[[[(1-Aminocyclopropyl)methyl](2-hydroxyethyl)amino]methyl]-2-chloro-N-(tricyclo[3.3.1.1^{3,7}]dec 1-ylmethyl) benzamide,
- 5-[[(2-Hydroxyethyl)[2 (methylamino)ethyl]amino]methyl]-2-methyl-N-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-benzamide,
- 2-Chloro-5-[3-[[2-(1-methyl-1H-imidazol-4-yl)ethyl]amino]propyl] N-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)benzamide,
- 2-Chloro-5-[3-[[2-(1H-imidazol-4-yl)ethyl]amino]propyl]-N-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)benzamide, and
- 2-Chloro-5-[3-[[3-(1H-imidazol-1-yl)propyl]amino]propyl]-N-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)benzamide.

Claim 11 (currently amended and reformatted): A process for the preparation of a compound of formula (I) as defined in claim 1 which comprises:

Page 13

(a) when X represents an oxygen or sulphur atom or a group NR ¹³, reacting a compound of general formula

$$R^2$$
 R^4 - L^1
 R^1
(III)

wherein L^1 represents a leaving group and D, E, R^1 , R^2 and R^4 are as defined in formula (I), with a compound of general formula

wherein R⁵ and R¹³ are X' represents an oxygen or sulphur atom or a group NR R¹³, and R⁵ is as defined in formula (I), optionally in the presence of a suitable silver salt; or

(b) when X represents SO or SO₂, reacting a corresponding compound of formula (I) in which X represents a sulphur atom with a suitable oxidising agent; or

(b)(c) when X represents a group NR R¹³, reacting a compound of general formula

ATTORNEY DOCKET NO.: 056291-5103-01 Continuation of Application No.: 10/149,549 Page 14

wherein R^{20} represents a bond or C_1 - C_5 alkyl group and D, E, R^1 and R^2 are as defined in formula (I), with a compound of general formula (VI) as defined in (a) above

$$\frac{H_{N}R^{5}}{R^{13}} = \frac{(VI);}{(VI)}$$

wherein R⁵ and R¹³ are as defined in formula (I), in the presence of a reducing agent; and optionally after (a), or (b) or (c) converting the compound of formula (I) obtained to a pharmaceutically acceptable salt or solvate thereof.

Claim 12 (currently amended): A pharmaceutical composition comprising a compound of formula (I), or a pharmaceutically acceptable salt or solvate thereof, as claimed

in any one of claims 1-4, 6 and 10 1 to 10 in association with a pharmaceutically acceptable

adjuvant, diluent or carrier.

Claim 13 (currently amended): A process for the preparation of a pharmaceutical

composition as claimed in claim 12 which comprises mixing a compound of formula (I), or a

pharmaceutically acceptable salt or solvate thereof, as defined in any one of claims 1-4, 6 and

10-1-to-10 with a pharmaceutically acceptable adjuvant, diluent or carrier.

Claims 14-19 (cancelled).

Claim 20 (currently amended): A method of effecting immunosuppression which

comprises administering a therapeutically effective amount of a compound of formula (I), or

a pharmaceutically acceptable salt or solvate thereof, as claimed in any one of claims 1-4, 6

and 10-1 to 10 to a patient in need thereof.

Claim 21 (currently amended): A method of treating rheumatoid arthritis which

comprises administering a therapeutically effective amount of a compound of formula (I), or

a pharmaceutically acceptable salt or solvate thereof, as claimed in any one of claims 1-4, 6

and 10-1 to 10 to a patient in need thereof.

Claim 22 (currently amended): A method of treating chronic obstructive pulmonary

disease which comprises administering a therapeutically effective amount of a compound of

1-WA/2165244.1

ATTORNEY DOCKET NO.: 056291-5103-01

Continuation of Application No.: 10/149,549

Page 16

formula (I), or a pharmaceutically acceptable salt or solvate thereof, as claimed in any one of claims 1-4, 6 and 10-1 to 10 to a patient in need thereof.